A-54528-7 PATENT

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

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| **Applicant** | : Berman et al. | Group Art Unit 1813 |
| **Serial N°** | : 171,858 | |
| **Filed** | : December 21, 1993 | |
| **For** | : VACCINES BASED ON MEMBRANE BOUND PROTEINS AND PROCESS FOR MAKING THEM | |
| **Examiner** | : L. Smith | |

# DECLARATION OF MICHEL DE WILDE

I, Michel De Wilde, hereby declare :

1. I am Vice-President & Director Research and Development, SmithKline Beecham Biologicals.

2. Significant progress has been made towards the commercial exploitation of the present invention.

3. Following receipt of a mammalian cell line expressing truncated gD of the present invention, SmithKline Beecham scientists developed a purification process for the molecule and demonstrated its efficacy in the guinea pig model. This model is regarded as the best predictor of HSV in humans.

4. Thereafter, process development at scale-up work was initiated. We have now reached the scale of 300 liter fermentors, as planned for manufacture of commercial lots. Corresponding downstream processing work has also been substantially concluded.

5. To date, SmithKline Beecham estimates that over $ 26,000,000 have been spent in preclinical and scale-up work.

6. Following positive results in preclinical tests, phase I and phase II clinical studies have been carried out. A total of 220 subjects have been enrolled in these studies, totalling 610 immunizations to date.

7. The target of these studies has been reached, that is, a level of immune response has been achieved comparable to natural infection with an excellent reactogenicity profile.

EXHIBIT E

8. Consequently, phase III efficacy studies have been designed to test efficacy in both therapeutic and prophylactic settings.

9. The therapeutic multicenter efficacy trial is ongoing in Canada and Sweden, and the prophylactic efficacy study is to start imminently in the United States, Canada , Australia, United Kingdom, Italy and Germany.

10. An IND was submitted to the United States FDA in May 1994. Supplemental information has since been provided to the FDA following questions on the clinical trial protocol.

11. Clinical development expenses to date are over $ 500,000 with an additional $ 3,000,000 engaged for the current efficacy studies (an additional 9 million are earmarked for further studies).

I declare that all statements made herein of my own knowledge are true, and that all statements made upon information and belief are believed to be true, and further, that these statements were made with the knowledge that willful, false statements and the like so made are punishable by fine or imprisonment, or both, under 18 U.S.C. $ 1001, and that willful, false statements may jeopardize the validity of the application or any patent issuing thereon.

Dated : July 26 th, 1994 By : _____
Michel DE WILDE